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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,415	02/19/2004	Antonio Marchetti	4239-67782	6397

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EXAMINER	
SEETHARAM, SARASWATHY	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/783,415	MARCHETTI ET AL.	
	Examiner	Art Unit	
	Saraswathy Seetharam, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *seq. compliance*.

5.00.

DETAILED ACTION

Claims 1-55 are cancelled.

Claims 56-66 are examined on their merits.

Sequence Requirements

In order to have compact prosecution a first office action can be performed on this application, however, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. Although the claims in the instant application are not drawn to specific sequences, the drawings in the disclosure contain sequences that need SEQ ID numbers on page 6 - Fig 5, line 24, page 8, Fig.11, line 21 and page 9, Fig.14, line 11. Applicant is reminded to check the entire disclosure to ensure that the application is in sequence compliance.

Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

APPLICANT IS GIVEN THE TIME ALLOTED IN THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six-month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 101/112

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56, 63 and 64 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

The claims as written, do not sufficiently distinguish over antibodies as they exists naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed antibodies and binding compositions and the structure of naturally occurring antibodies.

In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" antibody or similar language would obviate this rejection.

Claims 56-66 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

Claims 56-66 are directed to an antibody that specifically binds SEQ ID No. 4, or a fragment of the polypeptide encoded by a cDNA deposited under ATCC 97209 or 97030 that deregulates mammary epithelial cellular growth. The specification discloses the deduced sequences of murine and human *Int6* cDNA (SEQ ID No. 4) (pages 11 and 14). The proteins are disclosed to be identical (page 15, line 4). The specification states that all of the genes whose expression that have been affected by mouse mammary tumor virus integration in mouse mammary tumors have been highly conserved through evolution. The specification discloses the *Int6* gene in genomic DNA of C. elegans, Drosophila, Xenopus, chicken, mouse and human through southern blot analysis (Fig.6, example, 5). Further , the specification states that that the deduced amino acid sequence of the *Drosophila Int*6 protein is 60% identical to the human/mouse deduced amino acid sequences. Based on these results the instant application states that the evolutionary conservation of the Int6 gene , is indicative of *Int6* serving a basic life function. (page 48, lines 3-9). The specification teaches *Int6* specific mRNA expression in **a** tumor (tumor 178) (fig 4) and in all adult tissues (Figure 7a) and loss of mRNA expression in human lung and breast tumor samples (Figure 14 and 15). Further the specification discloses murine *in vitro* translation of *Int6* RNA in the rabbit reticulocyte system (example 15).

The instant claims are drawn to an antibody that specifically binds to a protein of SEQ ID No. 4, or its fragment that deregulates mammary epithelial cell growth. In order to fulfill the requirements of 35 U.S.C. 101, said binding of the said antibody to the polypeptide must be indicative of a specific, substantial and credible utility as the claimed deregulation of a pathological state of mammary epithelial growth. The specification does not provide any objective evidence on the expression of *Int6* protein in any of the human tissues specifically, the mammary tissue. The specification provides no teaching on binding of the said antibody to the polypeptide of *Int6* or to the protein of SEQ ID No. 4. The specification provides no teaching on the expression of the polypeptide of SEQ ID No. 4 on any established human or mouse mammary cell lines.

Based on the *Int6* mRNA expression in adult mouse target tissues and loss of this expression in human breast and lung tumor samples and structural identity with the mouse and *Drosophila* protein and the *in vitro* translation of RNA, the specification asserts that the

disclosed protein and the antibody have the same utility as the mouse and *Drosophila Int6* proteins.

The assertion that the disclosed protein has biological activities similar to known *Drosophila* and mouse *Int6* proteins is not substantial in the absence of supporting evidence, because the relevant literature reports numerous examples of polypeptide families wherein individual members have distinct, and even opposite, biological activities. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen *in vivo*, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- β family members BMP-2 and TGF- β 1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone14:717-720; see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48).

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also

echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Bowie et al. (1990, Science 247:1306-1310) state that determination of three dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (p. 1306). Thus, the specification fails to support the asserted, specific and substantial utility of deregulating mammary epithelial growth by the polypeptides of the instant application.

The specification does not support a substantial utility regarding the claimed polypeptide or the antibody that specifically binds the said polypeptide for purposes unrelated to the asserted biological activity. For example, the specification does not teach an altered level of expression of the polypeptide of SEQ ID NO.4. The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polypeptides. Also, the specification does not predict whether the claimed polypeptides and the antibody binding to would be to a specific, diseased tissue compared to the healthy tissue control.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed polypeptides. "Congress intended that no patent be

granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

Thus, one skill in the art would conclude that absence evidence that the polypeptide is expressed at an elevated level one would conclude that claimed invention is not supported by either a substantial asserted utility or a well established utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 62 recites the limitation " the kit of claim 62" in claim 66 which lacks antecedent basis in claim 62, because claim 62 recites "the antibody of claim 59, covalently linked to a detectable label" not " a kit". There is insufficient antecedent basis for this limitation in the claim.

Claim 56 is indefinite for reciting an antibody that specifically binds SEQ ID No:4, or a fragment of SEQ ID No:4 that "deregulates mammary epithelial growth" as the exact meaning of the words are not known. Claims 57-66 recite the antibody of claim 56. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said phrase. Since it is not clear how deregulation of the cell growth is measured there is no way for a person of skill in the art to ascribe a discrete method of identifying the function of the said phrase. Further, it is not clear whether "deregulation" means loss of expression or inappropriate expression of the polypeptide of SEQ ID No. 4. In addition, the term "deregulation" does not appear to be clearly defined in the specification whether it occurs *in vivo* and or *in vitro* under specific culture

environment ? Is it the function of the antibody that binds specifically to an epitope of the said polypeptide?

In the absence of a single art recognized meaning for the phrase and lacking a definition of the term in the specification, one of ordinary skill in the art could not determine the metes and bounds of the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56 –66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 56 is broadly drawn to an antibody that specifically binds the polypeptide of SEQ ID No. 4, or a fragment of SEQ ID No. 4 that deregulates mammary epithelial cell growth. Claims 57-63 are drawn to the antibody of claim 56 wherein the antibody is monoclonal, humanized, covalently linked to toxin , radionucleotide, a detectable label or drug, and a poly clonal antibody. Claim 54 recites the antibody of claim 56, wherein the antibody specifically binds the polypeptide encoded by a cDNA ,and claims 65 and 66 are drawn to a kit comprising the antibody of claim 56 and a second antibody that is labeled and binds the antibody of claim 56.

While the specification in the instant application teaches detection of *Int-6* mRNA expression in CZECH mammary tumors and in target tissues and loss of expression in human breast and lung tumor samples, it does not teach the expression of the *Int6* protein and the antibody that specifically binds the polypeptide (examples 6, 7 and 14). The specification does not teach the deregulation of the mammary epithelial cell growth in primary or established

mammary cell lines. Further, the specification contemplates administration of the said protein and the antibodies to mammals against cancer (page 31,lines 3-12). There are no working examples or guidance pertaining to the expression of the polypeptide of SEQ ID No.4 in normal and disease state. Therefore , one of skill in the art would not know how to use the protein or antibody in detection.

The increased copy number of DNA does not provide a readily apparent use for the polypeptide, for which there is no information regarding level of expression, activity, or role in cancer. This is underscored by Pennica et al (PNAS 95:14717-14722, 1998) which provides an example where the copy number is amplified but the RNA expression is actually reduced.

Those of skill in the art, recognize that expression of mRNA, specific for a tissue type, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Further, Powell et al (Pharmacogenesis, 1998, Vol. 8, pp. 411-421, abstract) teach that mRNA levels for cytochrome P450 E1 did not correlate with the level of corresponding protein, and conclude that the regulation of said protein is highly complex. Vallejo et al (Biochimie, 2000, vol. 82, pp. 1129-1133, abstract) teach that no correlation was found between NRF-2 mRNA and protein levels suggesting post-transcriptional regulation of NRF-2 protein levels. These references serve to demonstrate that the analysis of levels of polynucleotide transcripts cannot be relied upon to anticipate levels of protein expression. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation.

Furthermore, the literature indicates that such results are to be evaluated very critically. For example, Hu et al (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than l-fold difference in mean expression

level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

In addition, Hanash S (Nature Reviews, Applied Proteomics Collection, pp.9-14,March 2005) states "no single type of molecular approach fully elucidates tumor behavior, necessitating analysis at multiple levels encompassing genomics and proteomics" (see abstract). Human tumors are more complex and heterogenous than expected, and are caused by defects in numerous pathways and factors at many levels and incorporation of different genome-scale global profiling are expected to lead to molecular-based classifications of cancer that transcend organ and tissue types and supercede classifications based on the expression patterns of genes with unknown functional significance as in the present case for SEQ ID No. 4(see pages 9 and 14).

Thus, the predictability of protein translation and its possible utility as a diagnostic are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Thus absent evidence of the protein's expression including the correlation to a diseased state, one of skill in the art would be unable to predictably use the polypeptides in any diagnostic setting without undue experimentation.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention as in the instant application and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology,

however, must be enabled with a specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claim.

Claim 64 is rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are known and readily available to the public; and reproducible from the written description.

It is unclear if the cDNA clones that produce the above mentioned polypeptide of SEQ ID No.4 having the exact chemical identity is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above clones or antibodies, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed clones nucleic acid sequence is an unpredictable event.

Therefore, it would require undue experimentation to reproduce the claimed polypeptides of the instant application. Deposit of the cDNA clones would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials. The specification lacks complete deposit information for the deposit of cDNA clones .It is not clear that cDNA clones possessing the identical properties of the above mentioned polypetides of SEQ ID No.4 known and publicly available or can be reproducibly isolated from nature without undue experimentation. The specification lacks deposit information for the cDNA clones producing the above mentioned polypeptides on which the instant claims depend. One of skill in

the art must know how to make and use the claimed polypeptides and it is not clear if the exact cell line producing the polypeptide can be made without undue experimentation.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

> If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:
(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:
(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and
(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit. If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the

biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. Applicant's attention is directed to In re: Lundak, 773 F. 2d.1216, 227 USPQ 90 (CAFC 1985) and 37 CRF 1.801-1.809 for further information concerning deposit practice.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Saraswathy Seetharam, PhD whose telephone number is 571-272-3113. The examiner can normally be reached between M-F ,8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saraswathy Seetharam, PhD
Examiner
Art Unit 1642

***

JASEMINE C. CHAMBERS
DIRECTOR
TECHNOLOGY CENTER 1600

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Application No._____

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE